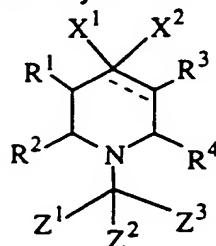


WHAT IS CLAIMED IS:

1. A compound represented by the formula



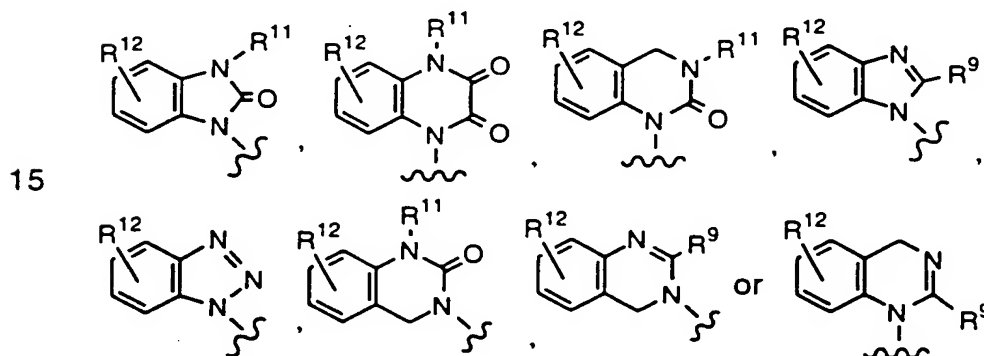
- 5 or a pharmaceutically acceptable salt or solvate thereof, wherein:

the dotted line represents an optional double bond;

X1 is R5-(C1-C12)alkyl, R6-(C3-C12)cycloalkyl, R7-aryl, R8-heteroaryl or R10-(C3-C7)heterocycloalkyl;

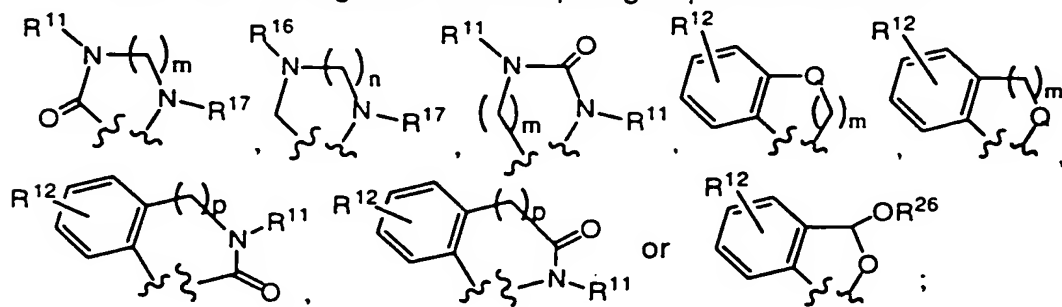
- 10 X2 is -CHO, -CN, -NHC(=NR26)NHR26, -CH(=NOR26), -NHOR26, R7-aryl, R7-aryl(C1-C6)alkyl, R7-aryl(C1-C6)alkenyl, R7-aryl(C1-C6)-alkynyl, -(CH2)vOR13, -(CH2)vCOOR27, -(CH2)vCONR14R15, -(CH2)vNR21R22 or -(CH2)vNHC(O)R21, wherein v is zero, 1, 2 or 3 and wherein q is 1 to 3 and a is 1 or 2;

or X1 is



and X2 is hydrogen;

or X1 and X2 together form a spiro group of the formula



- m is 1 or 2;
n is 1, 2 or 3, provided that when n is 1, one of R¹⁶ and R¹⁷ is -C(O)R²⁸;
p is 0 or 1;
5 Q is -CH₂-, -O-, -S-, -SO-, -SO₂- or -NR¹⁷-;
R¹, R², R³ and R⁴ are independently selected from the group consisting of hydrogen and (C₁-C₆)alkyl, or (R¹ and R⁴) or (R² and R³) or (R¹ and R³) or (R² and R⁴) together can form an alkylene bridge of 1 to 3 carbon atoms;
10 R⁵ is 1 to 3 substituents independently selected from the group consisting of H, R⁷-aryl, R⁶-(C₃-C₁₂)cycloalkyl, R⁸-heteroaryl, R¹⁰-(C₃-C₇)heterocycloalkyl, -NR¹⁹R²⁰, -OR¹³ and -S(O)₀₋₂R¹³;
R⁶ is 1 to 3 substituents independently selected from the group consisting of H, (C₁-C₆)alkyl, R⁷-aryl, -NR¹⁹R²⁰, -OR¹³ and -SR¹³;
15 R⁷ is 1 to 3 substituents independently selected from the group consisting of hydrogen, halo, (C₁-C₆)alkyl, R²⁵-aryl, (C₃-C₁₂)cycloalkyl, -CN, -CF₃, -OR¹⁹, -(C₁-C₆)alkyl-OR¹⁹, -OCF₃, -NR¹⁹R²⁰, -(C₁-C₆)alkyl-NR¹⁹R²⁰, -NH₂SO₂R¹⁹, -SO₂N(R²⁶)₂, -SO₂R¹⁹, -SOR¹⁹, -SR¹⁹, -NO₂, -CONR¹⁹R²⁰, -NR²⁰COR¹⁹, -COR¹⁹, -COCF₃, -OCOR¹⁹, -OCO₂R¹⁹,
20 -COOR¹⁹, -(C₁-C₆)alkyl-NHCOOC(CH₃)₃, -(C₁-C₆)alkyl-NHCOCF₃, -(C₁-C₆)alkyl-NH₂SO₂-(C₁-C₆)alkyl, -(C₁-C₆)alkyl-NHCONH-(C₁-C₆)alkyl or $-(CH_2)_f-N \begin{array}{c} \diagup \diagdown \\ \diagdown \diagup \end{array} N-R^{19}$, wherein f is 0 to 6; or R⁷ substituents on adjacent ring carbon atoms may together form a methylenedioxy or ethylenedioxy ring;
25 R⁸ is 1 to 3 substituents independently selected from the group consisting of hydrogen, halo, (C₁-C₆)alkyl, R²⁵-aryl, (C₃-C₁₂)cycloalkyl, -CN, -CF₃, -OR¹⁹, -(C₁-C₆)alkyl-OR¹⁹, -OCF₃, -NR¹⁹R²⁰, -(C₁-C₆)alkyl-NR¹⁹R²⁰, -NH₂SO₂R¹⁹, -SO₂N(R²⁶)₂, -NO₂, -CONR¹⁹R²⁰, -NR²⁰COR¹⁹, -COR¹⁹, -OCOR¹⁹, -OCO₂R¹⁹ and -COOR¹⁹;
30 R⁹ is hydrogen, (C₁-C₆)alkyl, halo, -OR¹⁹, -NR¹⁹R²⁰, -NHCN, -SR¹⁹ or -(C₁-C₆)alkyl-NR¹⁹R²⁰;
R¹⁰ is H, (C₁-C₆)alkyl, -OR¹⁹, -(C₁-C₆)alkyl-OR¹⁹, -NR¹⁹R²⁰ or -(C₁-C₆)alkyl-NR¹⁹R²⁰;
R¹¹ is independently selected from the group consisting of H,
35 R⁵-(C₁-C₆)alkyl, R⁶-(C₃-C₁₂)cycloalkyl, -(C₁-C₆)alkyl(C₃-C₁₂)cycloalkyl,

-(C₁-C₆)alkyl-OR¹⁹, -(C₁-C₆)alkyl-NR¹⁹R²⁰ and $-(\text{CH}_2)_q\text{-N} \begin{array}{c} \diagup \diagdown \\ \diagdown \diagup \end{array} \text{a}$,
 wherein q and a are as defined above;

R¹² is H, (C₁-C₆)alkyl, halo, -NO₂, -CF₃, -OCF₃, -OR¹⁹, -(C₁-C₆)alkyl-OR¹⁹, -NR¹⁹R²⁰ or -(C₁-C₆)alkyl-NR¹⁹R²⁰;

5 R¹³ is H, (C₁-C₆)alkyl, R⁷-aryl, -(C₁-C₆)alkyl-OR¹⁹, -(C₁-C₆)alkyl-NR¹⁹R²⁰ or -(C₁-C₆)alkyl-SR¹⁹;

R¹⁴ and R¹⁵ are independently selected from the group

consisting of H, R⁵-(C₁-C₆)alkyl, R⁷-aryl and $-(\text{CH}_2)_q\text{-C}(=\text{O})\text{-N} \begin{array}{c} \diagup \diagdown \\ \diagdown \diagup \end{array} \text{a}$,
 wherein q and a are as defined above;

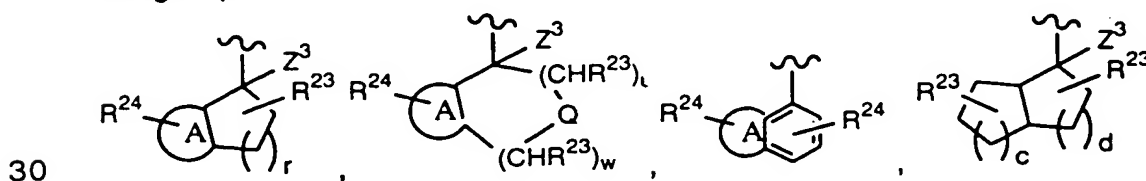
10 R¹⁶ and R¹⁷ are independently selected from the group consisting of hydrogen, R⁵-(C₁-C₆)alkyl, R⁷-aryl, (C₃-C₁₂)cycloalkyl, R⁸-heteroaryl, R⁸-heteroaryl(C₁-C₆)alkyl, -C(O)R²⁸, -(C₁-C₆)alkyl(C₃-C₇)-heterocycloalkyl, -(C₁-C₆)alkyl-OR¹⁹ and -(C₁-C₆)alkyl-SR¹⁹;

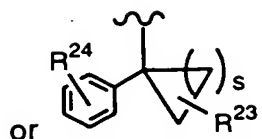
15 R¹⁹ and R²⁰ are independently selected from the group consisting of hydrogen, (C₁-C₆)alkyl, (C₃-C₁₂)cycloalkyl, aryl and aryl(C₁-C₆)alkyl;

20 R²¹ and R²² are independently selected from the group consisting of hydrogen, (C₁-C₆)alkyl, (C₃-C₁₂)cycloalkyl, (C₃-C₁₂)cycloalkyl(C₁-C₆)alkyl, (C₃-C₇)heterocycloalkyl, -(C₁-C₆)alkyl(C₃-C₇)-heterocycloalkyl, R⁷-aryl, R⁷-aryl(C₁-C₆)alkyl, R⁸-heteroaryl(C₁-C₁₂)alkyl, -(C₁-C₆)alkyl-OR¹⁹, -(C₁-C₆)alkyl-NR¹⁹R²⁰, -(C₁-C₆)alkyl-SR¹⁹, -(C₁-C₆)alkyl-NR¹⁸-(C₁-C₆)alkyl-O-(C₁-C₆)alkyl and -(C₁-C₆)alkyl-NR¹⁸-(C₁-C₆)alkyl-NR¹⁸-(C₁-C₆)alkyl;

R¹⁸ is hydrogen or (C₁-C₆)alkyl;

25 Z¹ is R⁵-(C₁-C₁₂)alkyl, R⁷-aryl, R⁸-heteroaryl, R⁶-(C₃-C₁₂)cycloalkyl, R¹⁰-(C₃-C₇)heterocycloalkyl, -CO₂(C₁-C₆)alkyl, CN or -C(O)NR¹⁹R²⁰; Z² is hydrogen or Z¹; Z³ is hydrogen or (C₁-C₆)alkyl; or Z¹, Z² and Z³, together with the carbon to which they are attached, form the group





or R^{24} , wherein r is 0 to 3; w and u are each 0-3, provided that the sum of w and u is 1-3; c and d are independently 1 or 2; s is 1 to 5; and ring A is a fused R^7 -phenyl or R^8 -heteroaryl ring;

R^{23} is 1 to 3 substituents independently selected from the group consisting of H, $(\text{C}_1\text{-C}_6)\text{alkyl}$, $-\text{OR}^{19}$, $-(\text{C}_1\text{-C}_6)\text{alkyl-OR}^{19}$, $-\text{NR}^{19}\text{R}^{20}$ and $-(\text{C}_1\text{-C}_6)\text{alkyl-NR}^{19}\text{R}^{20}$;

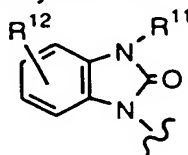
R^{24} is 1 to 3 substituents independently selected from the group consisting of R^{23} , $-\text{CF}_3$, $-\text{OCF}_3$, NO_2 or halo, or R^{24} substituents on adjacent ring carbon atoms may together form a methylenedioxy or ethylenedioxy ring;

R^{25} is 1-3 substituents independently selected from the group consisting of H, $(\text{C}_1\text{-C}_6)\text{alkyl}$, $(\text{C}_1\text{-C}_6)\text{alkoxy}$ and halo;

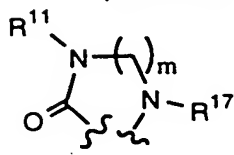
R^{26} is independently selected from the group consisting of H, $(\text{C}_1\text{-C}_6)\text{alkyl}$ and $\text{R}^{25}\text{-C}_6\text{H}_4\text{-CH}_2\text{-}$;

R^{27} is H, $(\text{C}_1\text{-C}_6)\text{alkyl}$, $\text{R}^7\text{-aryl}(\text{C}_1\text{-C}_6)\text{alkyl}$, or $(\text{C}_3\text{-C}_{12})\text{cycloalkyl}$;

R^{28} is $(\text{C}_1\text{-C}_6)\text{alkyl}$, $-(\text{C}_1\text{-C}_6)\text{alkyl}(\text{C}_3\text{-C}_{12})\text{cycloalkyl}$, $\text{R}^7\text{-aryl}$, $\text{R}^7\text{-aryl}(\text{C}_1\text{-C}_6)\text{alkyl}$, $\text{R}^8\text{-heteroaryl}$, $-(\text{C}_1\text{-C}_6)\text{alkyl-NR}^{19}\text{R}^{20}$, $-(\text{C}_1\text{-C}_6)\text{alkyl-OR}^{19}$ or $-(\text{C}_1\text{-C}_6)\text{alkyl-SR}^{19}$;



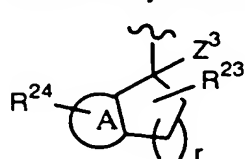
provided that when X^1 is or X^1 and X^2 together are



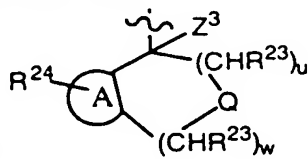
20

and Z^1 is $\text{R}^7\text{-phenyl}$, Z^2 is not hydrogen or $(\text{C}_1\text{-C}_3)\text{alkyl}$;

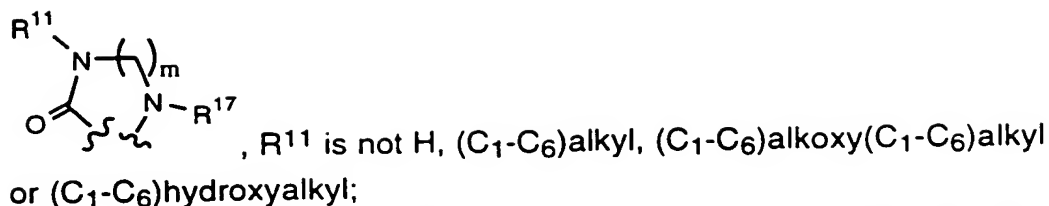
provided that when Z^1 , Z^2 and Z^3 , together with the carbon to which they are attached, form



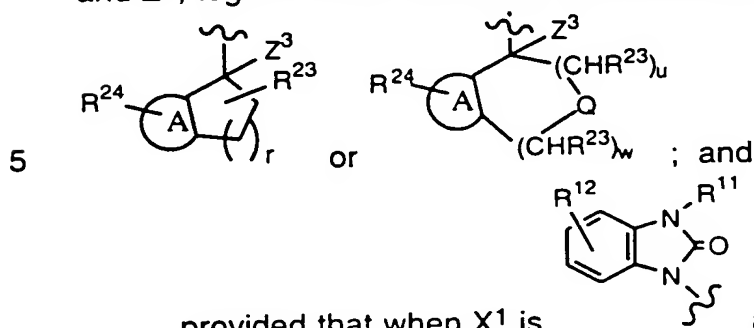
or



, and X^1 and X^2 together are

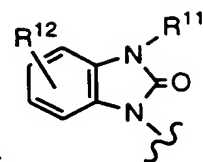


provided that when R² and R⁴ form an alkylene bridge, Z¹, Z² and Z³, together with the carbon to which they are attached, are not



provided that when X¹ is cycloalkyl, Z² is not H.

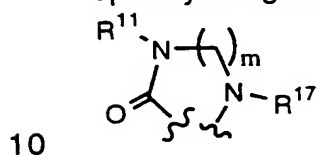
2. A compound of claim 1 wherein Z¹ and Z² are each R⁷-aryl.
- 10 3. A compound of claim 2 wherein Z¹ and Z² are each R⁷-phenyl.
4. A compound of claim 3 wherein R⁷ is selected from the group consisting of (C₁-C₆)alkyl and halo.
- 15 5. A compound of claim 1 wherein R¹, R², R³ and R⁴ are each hydrogen.
6. A compound of claim 1 wherein R¹ and R³ are each hydrogen
- 20 and R² and R⁴ are an alkylene bridge of 2 or 3 carbons.
7. A compound of claim 1 wherein X¹ is R⁷-aryl and and X² is OH or -NC(O)R²⁸.
- 25 8. A compound of claim 7 wherein X¹ is R⁷-phenyl.



9. A compound of claim 1 wherein X¹ is hydrogen. and X² is

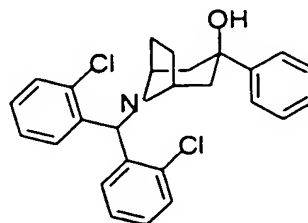
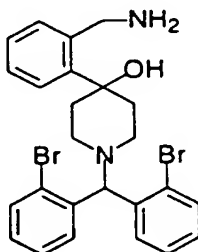
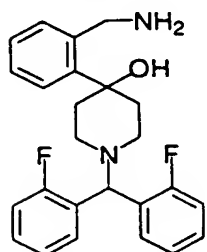
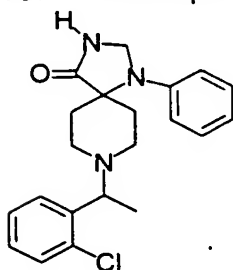
10. A compound of claim 9 wherein R¹² is hydrogen and R¹¹ is (C₁-C₆)alkyl, -(C₁-C₆) alkyl(C₃-C₁₂)cycloalkyl, -(C₁-C₆)alkyl-OR¹⁹ or -(C₁-C₆)alkyl-NR¹⁹R²⁰.

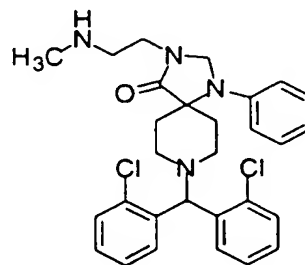
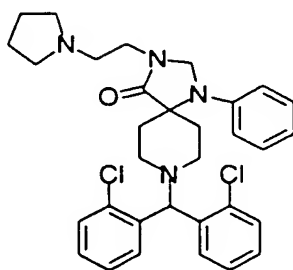
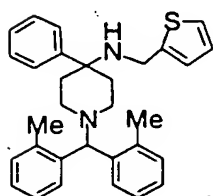
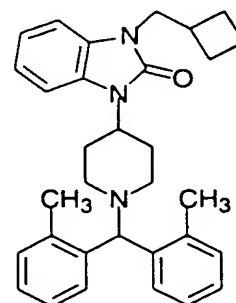
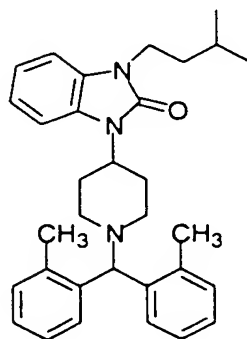
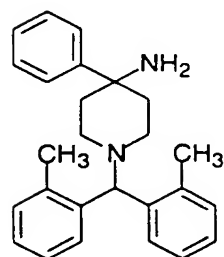
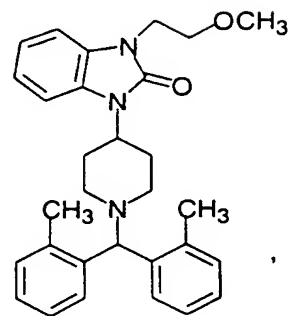
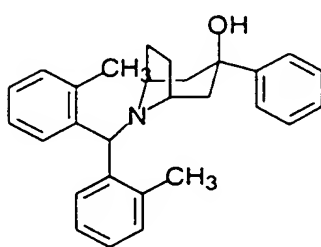
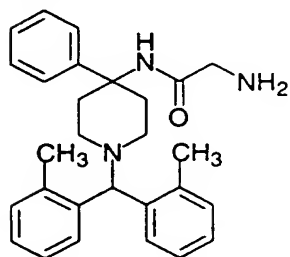
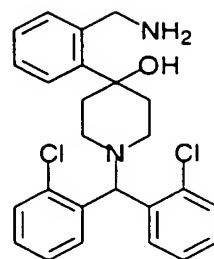
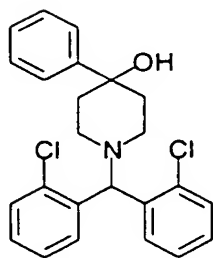
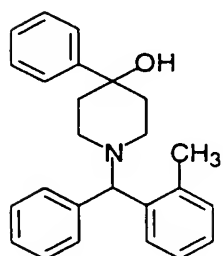
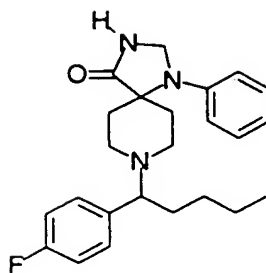
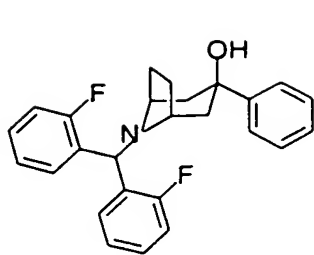
11. A compound of claim 1 wherein X¹ and X² together form the spirocyclic group

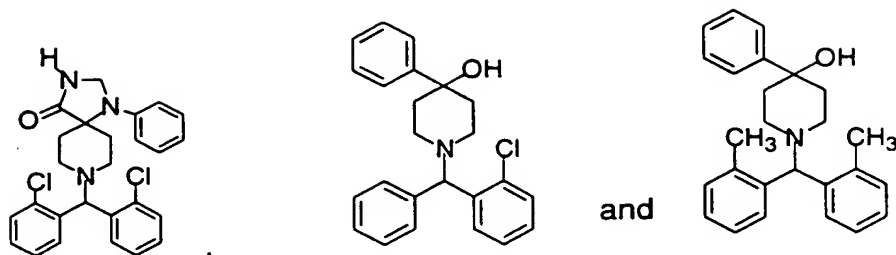


12. A compound of claim 11 wherein m is 1, R¹⁷ is phenyl and R¹⁶ is -(C₁-C₆)alkyl-OR¹⁹ or -(C₁-C₆)alkyl-NR¹⁹R²⁰.

15 13. A compound selected from the group consisting of







14. A pharmaceutical composition comprising a therapeutically effective amount of compound of claim 1 in combination with a
5 pharmaceutically acceptable carrier.

15. A pharmaceutical composition comprising: a therapeutically effective amount of a nociceptin receptor ORL-1 agonist; a therapeutically effective amount of a second agent selected from the
10 group consisting of: antihistamines, 5-lipoxygenase inhibitors, leukotriene inhibitors, H₃ inhibitors, β -adrenergic receptor agonists, xanthine derivatives, α -adrenergic receptor agonists, mast cell stabilizers, anti-tussives, expectorants, NK₁, NK₂ and NK₃ tachykinin receptor antagonists, and GABA_B agonists; and a pharmaceutically
15 acceptable carrier.

16. A method of treating pain, anxiety, asthma, depression or alcohol abuse comprising administering an effective amount of a compound of
20 claim 1 to a mammal in need of such treatment.

17. A method of treating cough comprising administering an effective amount of a nociceptin receptor ORL-1 agonist to a mammal in need of such treatment.

18. The method of claim 17, wherein in addition to the nociceptin receptor ORL-1 agonist, an effective amount of a second agent for treating cough, allergy or asthma symptoms selected from the group consisting of: antihistamines, 5-lipoxygenase inhibitors, leukotriene inhibitors, H₃ inhibitors, β -adrenergic receptor agonists, xanthine
25 derivatives, α -adrenergic receptor agonists, mast cell stabilizers, anti-tussives, expectorants, NK₁, NK₂ and NK₃ tachykinin receptor antagonists, and GABA_B agonists is administered.
30